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Comments on the Draft Guidance for Industry Pharmacogenomic Data Submission

Research and Development Committee

Japan Pharmaceutical Manufacturers Association

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The Research and Development Committee of JPMA (JPMA R&D Committee)* greatly appreciate the efforts of the FDA to provide the draft Guidance for Industry Pharmacogenomic Data Submission which apparently has much significance.

The JPMA R&D Committee member companies*(we) intend to supply innovative drugs internationally. Eventually, the studies conducted by us as well as those by US companies would be affected by this guidance once enforced. Therefore, we sincerely hope our following comments and suggestions to be duly considered and incorporated into the final guidance.

1. Definitions of Biomarkers and Interpretation Criteria for Outcomes

? The definition and determination of Known Valid Biomarkers and Probable Valid Biomarkers are critical factors for the applicant or holder of an IND, NDA, or BLA. We would appreciate it if the FDA would express in the guidance when, how (such

as standards and procedures), and by whom the definitions of the Known and Probable Valid Biomarkers are established, revised, and made public for reference.

? The draft guidance describes that a Known Valid Biomarker must be widely agreed in the medical or scientific community concerning the physiologic, toxicological, pharmacological, or clinical significance of the results. What is the definition of 'widely'? Could a marker be considered as a Known Valid Biomarker if it is supported by such data as generated by multiple well-controlled studies or it is included in published reports, or it is recommended by medical association(s), or it is approved as an IVD (*in vitro* diagnostic)? We would suggest that the FDA state certain criteria for establishing Known Valid Biomarkers in the guidance.

? The distinction between Known Valid Biomarkers and Probable Valid Biomarkers is not yet clear. It would be very helpful if the FDA could provide a list of currently available examples of the markers in the guidance or by other means of publication. Examples of genomic data submissions would also serve as highly useful guide for the IND, NDA, or BLA applicant or holder. We would ask you to enhance the examples by such other means as voluntary participation of pharmaceutical companies in the studies sponsored by the FDA.

2. Validation of Biomarkers

? In the global development, we desire that the methods for validating biomarkers be essentially standardized among regions as a prerequisite for time- and cost-saving drug development. We would suggest that the FDA provide examples of methods for validation concerning experimental precision of pharmacogenomic data collection, data analysis and reliability, and other technical aspects.

3. Interpretation of Test Results with Biomarkers

? The corporate decision in a new drug development using genomic data would be greatly influenced by the definition of No Observable Effect Level (NOEL), in particular, at the time of transfer from pre-clinical to clinical stage. We would appreciate if the FDA would include comments on the application of NOEL in the genomic data assessment.

4. Format of Reports

? There are three types of reports: full data submission, abbreviated report, and synopsis. We hope the FDA to provide an outline (content and items) of the abbreviated reports and synopses.

5. Handling of Reports and Data after Submission

? We are deeply concerned as to how reports and data in Voluntary Genomic Data Submission (VGDS) are to be handled and what the potential outcome of the submission may be. We would appreciate it if the FDA would clarify in the guidance the purpose of the use of VGDS, possible measures to be taken against important results with reanalysis by the FDA, standards and procedures for communicating FDA's decisions and recommendations, and criteria and procedures for disclosing the results of reanalysis.

? When the FDA approves a new drug utilizing pharmacogenomic data for identifying potential responders (efficacy and/or toxicity), should following drugs of the same class need to repeat similar pharmacogenomic tests? How could we determine or learn the necessity of the tests: via written guidance or consultation with the FDA?

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